1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/25/08 has been entered.

2. Claims 1,3,8-15,20,21,23-37 are under consideration.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. The rejection of claims 1,3,8-15,20,21,23-37 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons elaborated in the previous Office Action is withdrawn in view of the amended claims and applicants arguments.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1,3,8-15,23-36 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Weidanz et al. (WO 99/18129) in view of Lebowitz et al. Applicants arguments have been considered and deemed not persuasive.

Weidanz et al. disclose a TCR Vbeta/Cbeta attached by a linker to a Valpha/Calpha wherein said construct is linked to human Ig C kappa constant regions (see claims 1-22 and page 17). Weidanz et al. disclose use of Calpha fragment or Cbeta fragment in said construct (see claims 4 and 5). Weidanz et al. teach that the Calpha can be up to 22 amino acids (see page 15, lines 26-28). Weidanz et al. disclose use of Cbeta fragments in said construct (see claim 4) wherein the optimal length would be determined by routine experimentation. Weidanz et al. disclose an in vivo method of treatment with said construct to treat disease mediated by pathogenic T cells (see claim 39, page 11). The TCR chains used in the chimeric protein are derived from pathogenic T cells in the patient (see page 11 and 22-26). Weidanz et al. disclose that the chimeric protein can be made in insect cells using baculovirus. The recitation of` a particular means wherein the baculovirus produced chimeric protein is made carries no patentable weight. Weidanz et al. teach polyvalent multimers of the aforementioned chimeric TCR wherein said molecules would have multiple constant region chains (see page 35, last paragraph). Weidanz et al. do not teach said method using the chimeric protein of claim 1 containing a Ig heavy chain constant region. Lebowitz et al. teach soluble high affinity chimeric TCR proteins that contain a TCR alpha and beta chains (Valpha plus Calpha and Vbeta plus Cbeta) attached to IgGamma1 heavy and kappa light chains (see Figure 1 and 2). A routineer would have prepared the protein using human constant region fragments for use in humans as per disclosed by Weidanz et al. using Ig heavy and light chains of Lebowitz et al. One of ordinary skill in the art would have been motivated to do so because Lebowitz et al. disclose that the advantages of using IgG scaffold (aka both heavy and light chain constant regions) in said chimeric constructs (se page 179, first column, first complete paragraph). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Weidanz et al. disclose an in vivo method of treatment with chimeric T cell receptors to treat disease mediated by pathogenic T cells which express said receptor and the construct used, except for a Ig heavy chain constant region whilst Lebowitz et al. teach soluble high affinity chimeric TCR proteins that contain a TCR alpha and beta chains attached to Ig heavy and light chains. One of ordinary skill in the art would have been motivated to do the aformentioned because Lebowitz et al. teach the advantages of using IgG scaffold (aka both heavy and light chain constant regions) in said chimeric constructs.

Regarding applicants comments about page 22 of Weidanz et al., the particular passage does not refer to obtaining cells from multiple patients for administration to a single patient, it refers to patients that are suffering from the particular diseases recited in said passage. The art recognizes that T cells recognize antigen in the context of MHC antigen and that the recipient MHC also influences the nature of the peptide recognized (because the immunogenic peptide must bind the recipient MHC antigen to be recognized by T cells). Thus, the particular passage would not be interpreted by a routineer as encompassing administration of cells from different patients because different patients would not have the same MHC restricted T cells which bound the same antigens. Furthermore, page 11 of Weidanz et al. states that the mammal is immunized against "TCR antigenic determinants that occur on the surface of T-cells (ie. targeted T cells) and which are implicated in "the pathogenic or otherwise undesirable immune response.". Thus, the TCR are derived from the patient to be treated. In addition, it is noted that the claims under consideration are open in scope and therefore would encompass administration of TCR from other patients. Furthermore, the method of Weidanz et al. requires that the administered TCR conjugates express Vbeta and Valpha from the patient because otherwise there would be no response to vaccination (aka wherein a response against pathogenic T cells in the patient was generated) (as per claim 39).

Regarding applicants comments, there is currently no limitation in the claims under consideration which precludes covalent linkage of the Valpha and Vbeta chains. Regarding applicants comments, Lebowitz et al. teach soluble high affinity chimeric TCR proteins that contain a TCR alpha and beta chains (Valpha plus Calpha and Vbeta plus Cbeta) attached to IgGamma1 heavy and kappa light chains (see Figure 1 and 2). A routineer would have prepared the protein using human constant region fragments for use in humans as per disclosed by Weidanz et al. using Ig heavy and light chains of Lebowitz et al. One of ordinary skill in the art would have been motivated to do so because Lebowitz et al. disclose that the advantages of using IgG scaffold (aka both heavy and light chain constant regions) in said chimeric constructs (se page 179, first column, first complete paragraph). Regarding applicants comments about Weidanz et al., pages 2-3, Weidanz et al. disclose the successful production of Ckappa containing TCR constructs. Said passages refer to problems that were overcome by the invention of Weidanz et al. Regarding applicants comments about use of insect cells, Weidanz et

al. disclose that the chimeric protein can be made in insect cells using baculovirus. There is zero evidence of record that such insect made proteins could not be used in humans. Regarding applicants comments about insect proteins, the MPEP section 716.01(c)II states:

>II. < ATTORNEY ARGUMENTS CANNOT TAKE THE PLACE OF EVIDENCE

The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant.

Regarding applicants comments about a Walsh reference, no such reference is of record and a copy of said reference has not been received so applicants comments regarding said reference have not been considered. However, the prior art discloses use of insect produced proteins and is as enabled for the use of insect proteins as is applicants specification. Regarding applicants comments about the Lebowitz et al. reference, Weidanz et al. disclose that constant regions of an Ig molecule can be used in TCR conjugates. In addition, claim 1 does not preclude use of full length Ig heavy chain. As per above, Weidanz et al. teach the claimed method of treatment.

Regarding applicants comments, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Weidanz et al. disclose an in vivo method of treatment with chimeric T cell receptors to treat disease mediated by pathogenic T cells which express said receptor and the construct used, except for a Ig heavy chain constant region whilst Lebowitz et al. teach soluble high affinity chimeric TCR proteins that contain a TCR alpha and beta chains attached to Ig heavy and light chains. One of ordinary skill in the art would have been motivated to do the aformentioned because Lebowitz et al. teach the advantages of using IgG scaffold (aka both heavy and light chain constant regions) in said chimeric constructs.

7. Claim 37 stands rejected under 35 U.S.C. 103(a) as being unpatentable over as Weidanz et al. in view of Lebowitz et al. applied to claims 1,3,8-15,23-36 above, and further in view of Brostoff et al. (WO 94/25063). Applicants arguments have been considered and deemed not persuasive.

The previous rejection renders obvious the claimed method except wherein it can be used to treat T cell lymphoma. Brostoff et al. teach treatment of T cell lymphoma by administration of TCR derived from a T cell lymphoma (see page 2, last paragraph, continued on next page and page 3, last paragraph, continued on next page). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Weidanz et al. disclose an in vivo method of treatment with chimeric T cell receptors to treat disease mediated by pathogenic T cells which express said receptor and Brostoff et al. teach treatment of T cell lymphoma (a T cell mediate pathology) by administration of TCR derived from a T cell lymphoma (see page 2, last paragraph, continued on next page and page 3, last paragraph, continued on next page). One of ordinary skill in the art would have been motivated to do the aformentioned because Brostoff et al. teach treatment of T cell lymphoma (a T cell mediate pathology) by administration of TCR derived from a T cell lymphoma.

Regarding applicants comments about Brostoff et al., Brostoff et al. disclose that the TCR used can be isolated from the treated patient (see page 14, last paragraph, continued on next page). Regarding applicants comments about Brostoff et al., pages 11-12, said passages refer to the prior art use of vaccination with T cells. Said passages are irrelevant to the claimed invention (aka method that uses T cell immunoconjugates) and are equally irrelevant to the disclosure of Brostoff et al. which is not drawn to the use of T cells. Furthermore, even if Brostoff et al. did not teach that the TCR could be derived from the treated patients, the only way the treatment would have any effect would be if the molecule used were found on patient T cells (aka "associated with a particular TCR from a T cell from said patient"). In addition, it is noted that the claims under consideration are open in scope and therefore would encompass administration of TCR from other patients. Furthermore, the method of Brostoff et al. requires that the administered TCR conjugates express Vbeta and Valpha from the patient because otherwise there would be no response to vaccination (aka

wherein a response against pathogenic T cells in the patient was generated) (as per abstract).

8. Claims 20,21 are rejected under 35 U.S.C. 103(a) as being unpatentable over as Weidanz et al. in view of Lebowitz et al. applied to claims 1,3,8-15,23-36 above, and further in view of Bonnem et al. (WO 94/01133).

The previous rejection renders obvious the claimed method except wherein said method can be used with GM-CSF. Bonnem et al. disclose that GM-CSF can be administered to increase the immune response to an administered antigen (see claim 1 and abstract). Weidanz et al. disclose that their method can act by immunizing humans against pathogenic T cells which express the target TCR (see page 6, last paragraph). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Weidanz et al. disclose that their method can act by immunizing humans against pathogenic T cells which express the target TCR whilst Bonnem et al. disclose that GM-CSF can be administered to increase the immune response to an administered antigen. On of ordinary skill in the art would have been motivated to do the aformentioned because Bonnem et al. disclose that GM-CSF can be administered to increase the immune response to an administered antigen.

Applicants arguments are as per addressed above.

9. No claim is allowed.

10. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ron Schwadron, Ph.D./
Primary Examiner
Art Unit 1644